HYPERTENSIVE ENCEPHALOPATHY: BETWEEN DIAGNOSTIC ERROR AND REALITY

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ABSTRACT

Arterial hypertension is one of the most common and widespread disorders of the adult. Less than 1% of patients experience a hypertensive crisis. Hypertensive crisis is classified as hypertensive emergency or hypertensive urgency. Hypertensive encephalopathy, an acute cerebral event due to a marked elevation in arterial pressure, is one of the main vital complication of neglected hypertensive crisis. The goal of the author is to eliminate some practical confusion and to make this entity easier to recognize and treat.

Key words: arterial hypertension, hypertensive crisis, hypertensive encephalopathy

Arterial hypertension is one of the most common and widespread disorders of the adult. Both in Europe and in the United States, arterial hypertension is the first diagnosis made in the family doctors' practices. Worldwide, there are approximately 1 billion people with hypertension: about half are not being treated, and of those treated half are treated incorrectly (Vasan, RS et al., 2002).

The prevalence and social costs of arterial hypertension and its complications in our country are difficult to estimate, but preliminary data show that in the pilot hospitals uncomplicated hypertension is the first diagnosis upon admission. Mortality from arterial hypertension has risen from 72 per 100000 persons in 1980 to almost 95 per 100000 persons in 1999 (Conference of the Institute for the Management of Health Services, Sinaia 2002).

Its natural history, especially if neglected, culminates with acute cerebral, arterial and cardiac complications, which frequently develop on the background of some chronic, insidiously occurring complications. If ischemic or hemorrhagic stroke and the cardio-arterial complications are topics of frequent debates, both the medical community and the general population being aware of them, hypertensive encephalopathy, a more uncommon syndrome, is often unrecognized or incorrectly diagnosed in current practice. The goal of this paper is to eliminate some confusion and to make this entity easier to recognize and treat.

Hypertensive encephalopathy is an acute cerebral event due to a marked elevation in arterial pressure. For its understanding and correct diagnosis a consensus on the classification of the forms of arterial hypertension and hypertensive emergencies inducing or not organic lesions is essential.

Hypertensive emergencies are clinical conditions in which the sudden elevation in arterial pressure causes important lesions in the target organs: central nervous system, cardiovascular system, and kidneys.

The terms used to define these clinical situations have varied with time. Today, most authors believe that the term "hypertensive urgencies" should be reserved for the patients with an acute, severe elevation in arterial pressure without acute organ lesions, while "hypertensive emergencies" imply the presence of organ lesions not directly related to the absolute arterial pressure level. In practice, a clinical differentiation of "hypertensive emergencies" from "hypertensive urgencies" based on the absence ("urgency") or presence ("emergency") of target organ lesions is imperative as sometimes between the two of them there might be a continuum that makes them difficult to differentiate (Chobanian AV et al, 2003). Both clinical situations imply an acute and severe elevation in arterial pressure with SBP > 180 mm Hg and DBP > 110 mm Hg, the elevation rate rather than the absolute arterial pressure level being more important (Alper AB, 2002).

The two clinical forms also differ therapeutically: while hypertensive emergency requires measures to promptly reduce arterial blood pressure levels in order to prevent the occurrence of major complications, in hypertensive urgency arterial blood pressure control can be obtained within hours or days, most often using oral drugs.

Other authors use in defining the acute tensional events such terms as "malignant arterial hypertension" and "benign arterial hypertension with acute organ dysfunctions".

Malignant arterial hypertension is a clinical syndrome characterized by a marked elevation in arterial blood pressure accompanied by generalized, acute, diffuse arteriolar damage (hypertensive vasculopathy). The diffuse vascular lesion is evident at the fundus of the eye examination, which shows specific changes, known as hypertensive neuroretinopathy: flame-shaped retinal hemorrhages, soft exudates and sometimes papilledema. Malignant hypertension cannot be diagnosed in the absence of fundiscopic changes suggestive of renal, cardiac or brain involvement. Blood pressure lowering becomes emergent in order to avoid these complications.

In benign hypertension, without neuroretinopathy, the marked elevation in arterial blood pressure can be associated with marked acute organ damage. A moderate but sudden blood pressure elevation may compromise the target organ function in previously normotensive patients (ex. in preeclampsia or acute glomerulonephritis). Contrary, the patients with a long history of hypertension may tolerate even severe blood pressure elevations with less significant risk of organ damage as a result of the chronic anatomic changes of the arteriolar wall.

No matter of the used terms, it should be kept in mind that a marked blood pressure elevation associated with specific changes at the fundus of the eye examination determines acute organ damage favoring the occurrence of hypertensive encephalopathy.

Hypertensive encephalopathy is a term introduced in medical practice by Oppenheimer and Fishberg in 1928 to describe the changes occurring at encephalon level when elevated blood pressure determines a hypertensive vasculopathy progressing to intracerebral edema. It describes a series of transient, migratory neurologic symptoms associated to malignant hypertension (from hypertensive emergency) or benign hypertension with acute complications. The symptoms are frequently reversible under prompt treatment and require a complex differential diagnosis ab initio.

PATHOGENESIS OF HYPERTENSIVE ENCEPHALOPATHY

Physiologically, blood pressure elevation determines the activation of cerebral microcirculation self-regulation (vasoconstrictive response to arterioral wall distension), the cerebral blood flow remaining constant for a quite large area of cerebral perfusion ranging between 60 and 120 mmHg. When blood pressure elevation is sudden, reflex vasoconstriction is overcome and vasodilation of cerebral arterioles resulting in endothelial damage, extravasation of plasma proteins, cerebral hyperperfusion and cerebral edema occur, pathologic changes characteristic of hypertensive encephalopathy. The persistence of elevated endovascular pressure in malignant hypertension induces fibrinoid necrosis of arterioles and small arteries, and alteration of circulating red cells in the vessels occluded by fibrin deposits, resulting in the occurrence of a microangiopathic hemolythic anemia.

In the patients with chronic arterial hypertension, the arteriolar wall structural lesions cause a reset of mean arterial pressure at values of 110-190 mm Hg leading to a change in cerebral self-regulation curve so that these patients may tolerate elevated pressures. This phenomenon accounts for the clinical observation that hypertensive encephalopathy occurs at lower blood pressure levels in apparently normotensive patients than in those with chronic arterial hypertension.

In this process of cerebral circulation self-regulation loss, endothelium plays an essential role. Arterial wall tone is modulated by the interaction between endothelium and smooth muscle cells. Endothelium secretes nitric oxide (vasodilator), prostacyclin, and vasoactive substances that modulate vasoconstriction (Vougham CJ et al, 2000). The activation of renin-angiotensin-aldosteron system that leads to the major pressure elevation, reduces NO synthesis and the compensatory ability of the endothelium. Thus, a chain reaction is triggered, continuing arterial pressure elevation, release of inflammatory cytokines, fibrinoid arteriolar necrosis that will determine the loss of self-regulation function and target organs ischemia (Alper AB et al, 2002).

Any conditions predisposing a patient to sudden elevated blood pressure can cause hypertensive encephalopathy

CAUSES OF HYPERTENSIVE ENCEPHALOPATHY

- Malignant hypertension of any cause
- Acute glomerulonephritis, especially postinfectious
- Eclampsia
- Catecholamine-induced hypertensive crises
- Pheochromocytoma
- Monoamine oxidase inhibitor–tyramine interactions

- Abrupt withdrawal of centrally acting a 2 - agonists
- Cocaine-hydrochloride or alkaloid (crack cocaine) intoxication
- Acute lead poisoning in children
- High-dose cyclosporine for bone marrow transplantation in children
- Femoral lengthening procedures
- Acute renal artery occlusion from thrombosis or embolism
- Atheroembolic renal disease (cholesterol embolization)
- Recombinant erythropoietin therapy
- Transplantation renal artery stenosis
- Acute renal allograft rejection
- Paroxysmal hypertension in acute or chronic spinal cord injuries
- Post-coronary artery bypass or post-carotid endarterectomy hypertension

SYMPTOMS

The onset of symptoms is usually slow, with neurologic progression over 24-48 hours. Severe headache, blurred vision, nausea, vomiting, altered awareness (from confusion to coma), transient, nonfocal neurologic signs (nystagmus) are the neurologic manifestations of hypertensive encephalopathy. If hypertension is not controlled immediately, the outcome is usually fatal within a few hours. The neurologic manifestations may be accompanied by multiorgan damage: retinopathy with papilledema, instable angina, myocardial infarction, acute cardiac insufficiency, aortic dissection, kidney failure with oliguria or hematuria. Recently, Moorthy S et al. have described the "syndrome of reversible posterior encephalopathy", in which the described symptoms are associated with convulsions and MRI images of cortico-subcortical parieto-occipital edema syndrome that may be also determined by other medical causes than hypertensive emergencies like immunosuppresive therapy, eclampsia, acute renal failure, etc. (Moorthy S et al., 2002).

The neuroimaging changes seen in hypertensive encephalopathy (bilateral increase in T2 signal intensity in the white matter on MRI and a corresponding reduced density on CT) prevalently in the posterior hemisphere are due to cerebral edema that does not have a mass effect unlike other cerebral lesions (Ropper A, Brown R, 2005).

Differential diagnosis has to rule out an ischemic or hemorrhagic stroke, acute thrombotic stroke, intracranial hemorrhage, encephalitis, acute renal failure, intracranial hypertension, CNS mass lesion, conditions that may occur concomitantly with elevated blood pressure or may have similar symptoms. Improvement of mental status once blood pressure is controlled confirms the diagnosis of hypertensive encephalopathy (Yatsu FM, 2005).

TREATMENT

The reduction of high arterial blood pressure, according to patient's blood pressure levels prior to the neurologic event, should be done under constant monitoring and drug titration, possibly in an intensive care unit or stroke unit, the arterial pressure being measured by intraarterial catheter. This treatment aims at lowering the arterial blood pressure by 25% within 1-2 hours and the diastolic pressure to 100-110 mm Hg. If with the lowering of arterial blood pressure the neurologic status deteriorates the therapeutic scheme or the diagnosis should be reconsidered. Of the rapid- acting intravenous antihypertensive agents only labetalol, sodium nitroprusside and phenoldopam (in kidney failure) have proved to be effective in hypertensive encephalopathy.

Labetalol, a beta-adrenergic blockers, seems to be the most adequate as it does not lower the cerebral blood flow and acts within 5 minutes of administration. The initial dose is 20 mg administered as a bolus dose, then 20-80 mg intravenous doses every 10 minutes until the goal blood pressure or a maximum total dose of 300 mg of reached.

Sodium nitroprusside, a vasodilator, has a rapid onset of action (seconds) and a short duration of action (1-2 minutes). However, it can induce an important cerebral venodilatation with a possibly resulting increase in cerebral blood flow and intracranian hypertension. A cytotoxic action, by the release of NO, free radicals, is suspected, and its metabolic products, cyanides, can generate sudden death, or comatose states. The initial dose is 0,3-0,5 mcg/kg/min IV, adjusting the infusion rates until the target effect is reached with mean doses of 1-6 mcg/kg/min.

Fenoldopam (Corlopam) is a short-acting dopamine agonist (DA1) at peripheral level, with a short duration of action. It increases renal blood flow and sodium excretion and can be used in patients with signs of kidney failure. The initial dose of 0,03 mcg/kg/min IV is progressively increased to the maximum of 1.6 mcg/kg/min.

Nicarpidine as a bolus dose of 5-15 mg/h IV and a maintenance dose of 3-5 mg/h can also be used.

Sublingual nifedipine, clonidine, diazoxide or intravenous hydralazine are not recommended as they may induce an uncontrolled lowering of arterial blood pressure with resulting cerebral and renal ischemia.

Further management of arterial blood pressure is essential for patient's future known being the fact that the patients with hypertensive emergencies have a mortality rate of 50% at 6 months and 90% at 1 year.

CONCLUSION

Even though the etiology, clinical manifestations and possible complications of hypertensive encephalopathy seem familiar, this entity remains an exclusion diagnosis that requires a rapid clarification and a few emergency investigations. Correct treatment is decisive. In the absence of a rapid diagnosis and initiation of a correct and prompt therapy, it may lead to cerebral infarctions, intracerebral hemorrhage, coma and death.

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